PATENT SPECIFICATION

1,040,724

NO DRAWINGS

1,040,724

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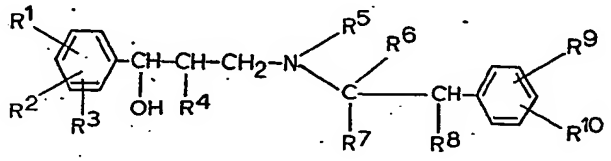
Int. Cl.:—C 07 c 91/16

COMPLETE SPECIFICATION

Process for the preparation of Amino Alcohols

We, DEUTSCHE GOLD-UND SILBER-SCHEIDEANSTALT VORMALS ROESSLER, a body corporate organised under the laws of Germany of 9 Weissfrauenstrasse, Frankfurt/Main, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to compounds of the general formula

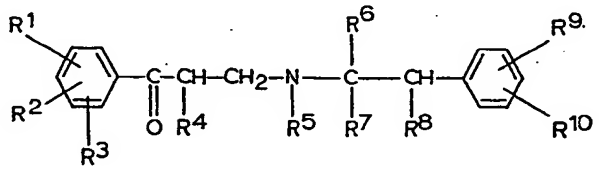


(I)

their salts and quaternary ammonium compounds and optically active isomers in which formula R^1, R^2, R^3, which may be the same or different are hydrogen or chlorine atoms or hydroxyl, methoxy or nitro groups, R^4 is hydrogen or a methyl or ethyl radical, R^5, R^6 and R^7, which may the same or different, are hydrogen or methyl radicals, R^8 is hydrogen or a hydroxyl group, R^9 and R^{10}, which may be the same or different are hydrogen, chlorine or methyl or methoxy radicals.

The new compounds are pharmaceutically valuable, particularly in the treatment of heart or circulatory diseases. They are outstandingly suitable for the improvement of cardiac functions.

The invention also provides processes for the production of compounds of the invention wherein a compound corresponding to the general formula



(II)

is reduced.

[1]

This reduction can be carried out in known manner by treatment with hydrogen in the presence of catalysts or using reducing agents such as sodium borohydride, lithium borohydride, alkali metal alcoholates, alkaline-earth metal alcoholates or aluminium alcoholate.

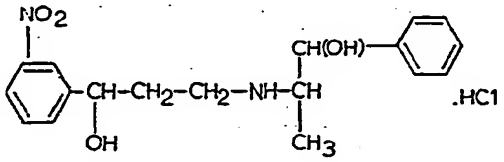
If required, the bases thus obtained can be converted into their salts or into their quaternary ammonium compounds.

These compounds, which also contain optically active carbon atoms and which are obtained, as a rule, in the form of racemates, can be reacted with an optically active acid and thereafter separated into their optically active isomers by fractionating precipitation or crystallisation. In many cases it is possible to use optically active starting materials.

The invention is further illustrated by the following Examples.

EXAMPLE 1.

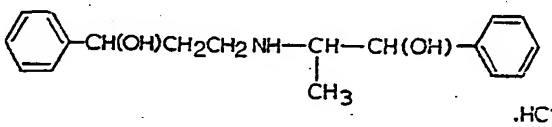
N - [3 - phenyl - 3 - hydroxy - propyl - (2)] - 3 - (3 - nitro - phenyl) - 3 - hydroxy-propylamine hydrochloride



4 g. of $NaBH_4$ dissolved in 30 ml. of water are added dropwise to a mixture of 25 g. of N - [3 - phenyl - 3 - hydroxy - propyl - (2)] - β - amino - 3 - nitro - propiophenone, produced from 1-Norephedrine and 250 ml. of methanol and the mixture is stirred at a temperature of 25°C. for 2 hours. The solvent is evaporated off and the residue taken up with benzene and shaken with a dilute sodium hydroxide solution. The benzene solution is dried and evaporated. The residue is converted into the hydrochloride and recrystallised three times from ethanol. The melting point is 217°C.

EXAMPLE 2.

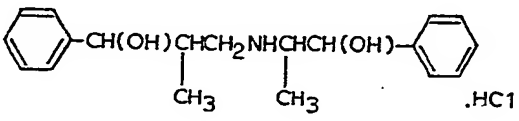
25 g. of 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1 - phenyl - propanone - (1). HCl are dissolved in 400 ml. methanol and hydrogenated with hydrogen at 60°C. and 10 atm. gauge pressure in the presence of 4 g. $Pd/BaSO_4$ (5% Pd) as catalyst. The solution is filtered and evaporated. The residue is taken up in 20 ml isopropanol and mixed with 130 ml other-petrolether. The 3 - [1 - phenyl - 1 - hydroxy-propyl - (2) - amino] - 1 - phenyl - propanol - (1). HCl



thus formed is recrystallised from isopropanol. Melting point 176—178°C.

EXAMPLE 3.

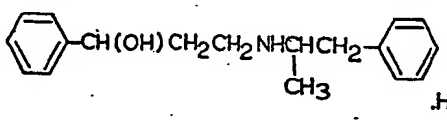
33.5 g. of 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1 - phenyl - 2-methyl - propanone - (1).HCl are dissolved in 500 ml. methanol and reduced at 60°C. and 10 atm. gauge pressure in the manner already described in Example 1. After reiterated recrystallisation from methanol there is obtained the hydrochloride of the 3-[1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1 - phenyl - 2 - methyl - propanol-(1).



melting at 239°C.

EXAMPLE 4.

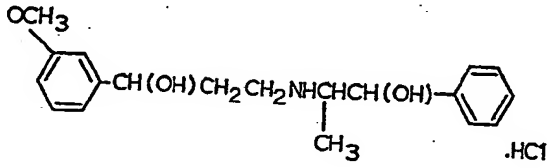
30.5 g. of 3 - [1 - phenyl - propyl - (2) - amino] - 1 - phenyl - propanone - (1). HCl are dissolved in 500 ml. methanol and reduced in the manner described in Example 1. The 3 - [-phenyl - propyl - (2) - amino] - 1 - phenyl - propanol - (1).HCl.



thus obtained is twice recrystallised from isopropanol ether and melts at 173°C.

EXAMPLE 5

20 g. of 3 - [phenyl - 1 - hydroxy - propyl - (2) - amino] - 1 - (*m* - methoxy-phenyl) - propanone - (1). HCl are dissolved in 500 ml. methanol and reduced. The 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1 - (*m* - methoxy - phenyl - propanol - (1).HCl.



thus formed melts at 155—158°C. after reiterated recrystallisation from isopropanol ether.

EXAMPLE 6.

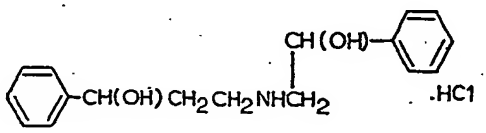
16 g. (0.05 mol) of 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino]-1 - phenyl - propanone - (1).HCl, dissolved in 100 ml methanol, are reacted at 25°C. with 2.9 g (1.5 × 0.05 mol) sodium borohydride which has been dissolved in 25 ml water. The mixture is stirred for one hour. The solution is hereafter concentrated, taken up in 100 ml of water, mixed with 40 ml of a 40% sodium hydroxide solution and extracted with benzene. The benzenic extract is dried with potassium carbonate and evaporated. The residue is dissolved in 25 ml of isopropanol and neutralised with isopropanolic hydrochloric acid. The salt precipitating is recrystallised from isopropanol-benzene. Melting point: 179°C.

EXAMPLE 7.

28.5 g (0.1 mol) 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1-phenyl-propanone - (1) - base, dissolved in 150 ml isopropanol, are heated with 20.4 g (0.1 mol) aluminium isopropylate to 80°C. for 8 hours, under stirring in a nitrogen stream. The solution is hereafter evaporated to dryness. The residue is dissolved in 80 ml of 20% sulphuric acid, rendered alkaline with sodium hydroxide and extracted with benzene. Melting point: 179°C.

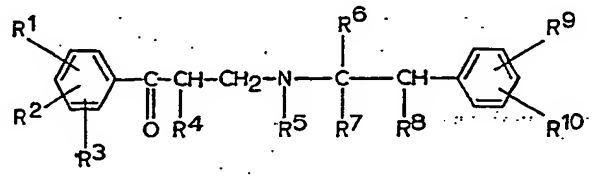
EXAMPLE 8.

N - (2 - phenyl - 2 - oxy - ethyl) - 3 - phenyl - 3 - oxy - propylamine. HCl



28 g. of N - (2 - phenyl - 2 - oxy - ethyl) - β - amino - propiophenone.HCl are dissolved in 500 ml methanol and hydrogenated at 60°C. and 10 atm. gauge pressure with 3 g. Pd-barium sulphate (5% Pd.). The solution is then filtered and evaporated *in vacuo*. The residue is recrystallised from an isopropanol-benzene mixture. Melting point: 193°C.

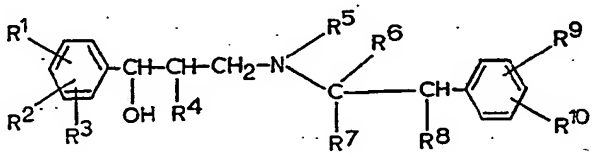
Our co-pending Application No. 11723/63 (Serial No. 1,040,722) describes and claims compounds of the general formula



in which the radicals R^1 to R^8 have the same meanings as the same radicals defined in this Specification, this co-pending Application also describes and claims a process for the producton of these compounds.

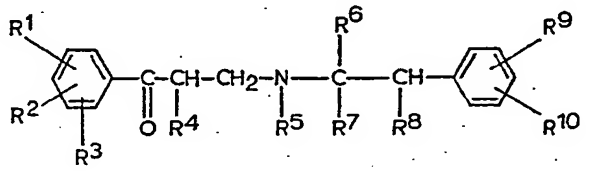
WHAT WE CLAIM IS:—

1. A process for the preparaton of compounds corresponding to the general formula



(I)

in which R^1, R^2 and R^3 are the same or different and represent a hydrogen or chlorine atom, a hydroxyl, methoxy or nitro radical, R^4 represents a hydrogen atom or a methyl or ethyl radical, R^5 represents a hydrogen atom or a methyl radical, R^6 and R^7 are the same or different and represent a hydrogen atom or a methyl radical, R^8 represents a hydrogen atom or a hydroxyl radical and R^9 and R^{10} are the same or different and represent a hydrogen or chlorine atom or a methyl or methoxy radical, wherein a compound corresponding to the general formula



(II)

is reduced.

2. A process as claimed in claim 1, wherein the resulting bases are converted into their salts or quaternary compounds as known *per se*.

3. A process as claimed in claim 2, wherein the resulting racemates are reacted with an optically active acid, the optically active isomers being obtained from such salts by fractional precipitation or crystallisation.

4. A process as claimed in claim 1, wherein optically active starting materials are used.

5. Compounds of general formula (I) as defined in claim 1.

6. N - [3 - phenyl - 3 - hydroxy - propyl - (2)] - 3 - (3 - nitro - phenyl) - 3-hydroxy - propylamine.HCl.

7. 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1 - phenyl - propanol-(1).HCl.

8. 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1 - phenyl - 2 - methyl-propanol - (1)HCl.

9. 3 - [1 - phenyl - propyl - (2) - amino] - 1 - phenyl - propanol - (1) HCl.

10. 3 - [1 - phenyl - 1 - hydroxy - propyl - (2) - amino] - 1-(*m*-methoxy-phenyl)-propanol - (1)HCl.

ELKINGTON AND FIFE,
Chartered Patent Agents,
High Holborn House, 52/54, High Holborn, London, W.C.1.
Agents for the Applicants.

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